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A Case-Control Study of Fluctuating Dermatoglyphic Asymmetry as a Risk Marker for Developmental Delay

Christopher T. Naugler and Mark D. Ludman

Medical Genetics, Department of Pediatrics, Dalhousie University and IWK Children's Hospital, Halifax, Nova Scotia, Canada

In traits which are normally bilaterally symmetrical, asymmetries may arise as a result of genomic or environmental stress. Such asymmetries are called fluctuating asymmetry. Symmetry is known to be decreased in a variety of disorders of developmental origin, and thus could potentially serve as a risk marker for disorders with a developmental component. We examined this idea by conducting a case-control study of 49 developmentally delayed children and 51 controls. Using two dermatoglyphic characters as a measure of symmetry (finger print concordance and A-B triradial ridge count difference), we found odds ratios of 2.32 (95% CI 0.65-3.17) and 2.11 (95% CI 0.57-3.27); depending on which character was measured. These results suggest that fluctuating asymmetry may have potential as a risk marker for developmental disorders, and that this area of research warrants further research. © 1996 Wiley-Liss, Inc.

KEY WORDS: fluctuating asymmetry, developmental delay, dermatoglyphics, risk marker

INTRODUCTION

Corresponding bilateral traits in humans are generally symmetrical, except for the visceral organs. Size discrepancies in normally symmetrical traits are thought to result from an inability of the individual to buffer environmental and/or genomic stress [Livshits and Kobyliansky, 1991; Clarke, 1992; Parsons, 1992]. These deviations from normal symmetry are known as "fluctuating" asymmetry. By definition, fluctuating asymmetry shows no preference for the same side in different individuals, and within a population is normally distributed with a parametric mean of zero [Van Valen, 1962]. If these same stresses play a role in the etiology of disorders of developmental origin, then high levels of fluctuating asymmetry may serve as a risk marker for developmental disorders. Indeed, increased fluctuating asymmetry has been reported in Down syndrome [Garn et al., 1970; Barden, 1980b; Townsend, 1983], fetal alcohol syndrome [Wilber et al., 1983], cleft lip [Woolf and Gianas, 1976, 1977], and fragile X syndrome [Peretz et al., 1988]. However, in these disorders, the association with increased fluctuating asymmetry does not aid in diagnosis and is therefore primarily of academic interest. Increased fluctuating asymmetry relative to controls has also been demonstrated in schizophrenia [Markow and Wandler, 1986; Markow and Gottesman, 1989; Mellor, 1992] and mental retardation [Barden, 1989a; Malina and Buschang, 1984], disorders in which fluctuating asymmetry could potentially aid in diagnosis. Unfortunately, in all studies we are aware of, only group comparisons have been reported. In order for fluctuating asymmetry to be useful in clinical diagnosis, we need to know its potential as a risk marker. One way to express this is through the use of odds ratios [Naugler and Ludman, 1996].

In this report, we use developmental delay in children as a model in which to explore the usefulness of fluctuating asymmetry as a risk marker. Psychomotor developmental delay encompasses a group of diagnoses of presumed developmental origin, and has the advantage of not being associated with specific characteristic phenotypic features. We assess fluctuating asymmetry by measuring dermatoglyphic traits [Livshits and Kobyliansky, 1987]. Dermatoglyphics are formed at approximately the 10th week of embryonic development [Penrose and Ohara, 1973] and are therefore probably most sensitive to environmental and genomic stresses acting in the early gestational period. Dermatoglyphics have the advantage of remaining stable throughout life and therefore can be compared among individuals of different ages. Dermatoglyphic print concordance has

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Address reprint requests to Dr. Mark D. Ludman, Medical Genetics, Department of Pediatrics, Dalhousie University, IWK Children's Hospital, PO Box 3070, 5850 University Avenue, Halifax, Nova Scotia, Canada, B3J 3G9.

the disadvantages of being a discrete rather that a continuous variable and of being sensitive to extreme shifts in the frequency of print types in certain groups. For example, the preponderance of ulnar loop patterns in Down syndrome [Rodewald, 1976] may result in misleadingly low fluctuating asymmetry estimates of finger print concordance in this group. Dermatoglyphics have been used by a number of previous writers to assess fluctuating asymmetry [e.g., Holt, 1954; Singh, 1970; Martin et al., 1982; Markow and Wandler, 1986; *Woolf and* Gianas, 1976, 1977; Markow and Gottesman, 1989; Mellor, 1992; Arrieta et al., 1993; Wilber et al., 1993].

METHODS

A case-control design was employed, using a sample of children diagnosed with developmental delay and a control group consisting of children without a diagnosis of developmental delay. The children with developmental delay were obtained through the Developmental Clinic at the Izaak Walton Killam (IWK) Children's Hospital between 13 November 1994 and 8 May 1995, and the controls were obtained through the Ear, Nose and Throat Clinic at the IWK Children's Hospital between 24 April 1995 and 8 May 1995. The inclusion criteria for this study was that developmentally delayed children must be outpatients of the IWK Developmental Clinic and must have had a diagnosis made. Controls must have been outpatients of the IWK ENT clinic. The exclusion criteria for developmentally delayed children was any major comorbid condition (e.g., Down syndrome, cerebral palsy, fetal alcohol syndrome, etc.) and for controls was a suspicion or actual diagnosis of developmental delay as evidenced by a prior assessment by the IWK Developmental Clinic.

The method of data collection was as follows. Individual children and their parent(s) or guardian were approached in the waiting area of one of the abovementioned clinics. We explained the study and asked the parent and child if they would like to participate. Participants were then asked to sign a release form. Fingerprints and partial palm prints were taken using a "Perfect Print" ink pad (Identicator Corporation). For children seen through the developmental clinic, any diagnoses were recorded from their chart after the prints were taken.

Each fingerprint was classified by type of print pattern according to standard dermatoglyphic nomenclature [see Cummins, 1961; Markow and Gottesman, 1989]. Print concordance was first assessed for each corresponding finger pair. If the corresponding fingers bore the same type of print pattern, that pair was given a score of one; if not, it was given a score of zero. These were then summed to give the total print concordance out of a maximum of five. Thus, an individual with whorls on both first fingers, ulnar loops on both third fingers, and different patterns between the left and right hands on the remaining three fingers would have received a finger print concordance score of two out of five. We also scored the A-B triradial ridge count difference, as described by Rose et al. [1987]. The child's age, sex, and diagnosis (if any) were also recorded.

We then chose cutoff values for these variables that appeared to give the maximum separation between the developmentally delayed and control groups. Odds ratios were calculated for both fingerprint concordance and A-B ridge count differences.

RESULTS

In total, 49 developmentally delayed children and 51 controls were obtained. Of the developmentally delayed children, 21 carried a diagnosis of learning or language disability, 20 were diagnosed with attention deficit hyperactivity disorder or attention deficit disorder, 6 were diagnosed with global developmental delay, and 2 were autistic. Three children from the Developmental Clinic were excluded because of other major comorbid conditions. No controls were excluded. One family from the Developmental Clinic and three from the ENT clinic chose not to participate.

Table I shows the sample sizes and demographic breakdown of the children in this study. Figure 1 shows the distribution of finger print concordance asymmetries for controls and children with developmental delay. The distribution for data on A-B triradial ridge count asymmetries is given in Figure 2. The sample sizes differ in the two figures because in five controls and two individuals with developmental delay, the A-B triradial ridge count could not be adequately quantified from the print. The means and standard deviations for each character are given in Table II.

Using a cutoff value for a fingerprint concordance of zero to three pairs the same versus four or five pairs the same, the odds ratio for the developmental delay group vs. the control group is 2.32 (95% confidence interval = 0.65-3.17). Thus, children with a finger print concordance of three or fewer are over twice as likely to have a diagnosis of developmental delay. Using a cutoff value of a difference in the A-B triradial ridge counts between left and right hands of four or greater vs. three or less, the odds ratio for the developmental delay group vs. the control group is 2.11 (95% confidence interval = 0.57-3.27). This indicates that children with an asymmetry of four or greater between the A-B ridge counts are approximately twice as likely to have a diagnosis of developmental delay.

Because the sex ratio is different in the developmentally delayed and control groups, we looked for differences in symmetry between females and males. We compared control males vs. control females and developmentally delayed males vs. developmentally delayed females for both print concordance and triradial ridge count differences and found no statistically significant differences for any of the comparisons (Mann-Whitney U-tests, all P values >0.05).

TABLE I. Demographics of Control and Developmentally Delayed Children

	Developmentally delayed group	Control group
Sample size	49	51
Mean age (years)	10.2	9.0
Sex ratio (M/F)	3.45	1.32

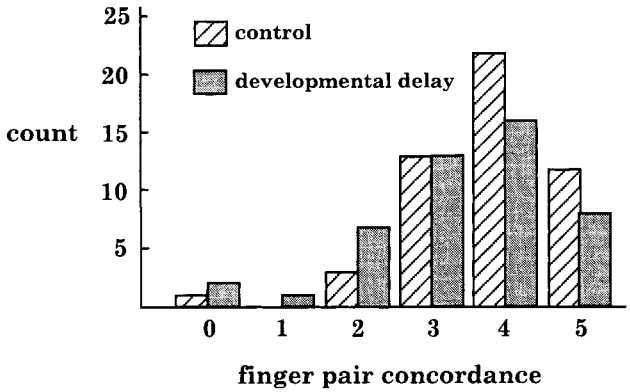

Fig. 1. Distribution of asymmetries in finger pair concordance (number of pairs of corresponding fingers in each individual with the same type of print pattern). See text for details of methodology.

DISCUSSION

We found that higher levels of fluctuating asymmetry suggested an increased risk of carrying a diagnosis of developmental delay, as assessed by odds ratios. Small sample sizes, however, resulted in large confidence intervals around the odds ratios. Thus, it appears that increased fluctuating asymmetry may represent a previously unrecognized risk marker for the appearance of developmental delay. This is important because at present the definitive diagnosis of developmental delay is often not clear until the child begins school, if not later. Because dermatoglyphics do not change throughout life, the potential exists to assess fluctuating asymmetry at an earlier age to increase or decrease the index of suspicion of developmental delay. Unfortunately, our sample size is insufficient to examine fluctuating asymmetry in individual developmental delay etiologies. Further analyses using more precise diagnostic categories is an obvious next step. Additional studies are also needed to examine the heritability of fluctuating asymmetry using parents and sibs as comparison control groups.

We would expect that with regard to finger print concordance, the mean should be higher in the control group (more symmetrical) and also that the variance should be less in the control group [Palmer and Strobeck, 1986]. Table II shows that this is indeed the case. However, the expected patterns did not hold true for A-B triradial ridge counts. We would expect that controls in this case would show a lower mean (less

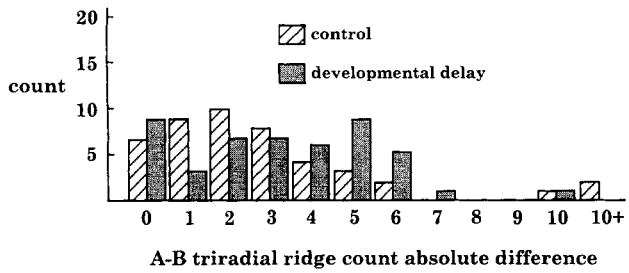

Fig. 2. Distribution of asymmetries between left and right hands in A-B triradial ridge counts. See text for details of methodology.

TABLE II. Descriptive Statistics of Dermatoglyphic Asymmetries Measured in Control and Developmentally Delayed Children

	Sample size	Mean	Standard deviation
Control Group			
Finger print concordance	51	3.78	1.006
A-B triradial ridge count asymmetry	48	3.48	5.009
Developmentally delayed group			
Finger print concordance	49	3.38	1.239
A-B triradial ridge count asymmetry	47	3.31	2.699

asymmetrical) as well as a lower variance. Instead, the mean of controls is lower and the variance is higher. Because of the small sample sizes, however, parametric descriptive statistics were strongly influenced by extreme outliers. In our analysis, two values fell well above the remainder of the distribution for controls (see Fig. 2). The actual values in these cases were 25 and 26. The one outlier for the developmental delay group had a value of 15 (see Fig. 2). If these values are removed the descriptive statistics for the controls become: mean = 2.52, s.d. = 2.158, and the descriptive statistics for the developmental delay group become mean = 3.06, s.d. = 2.010.

The control group used in this study consisted of children seen through the ENT clinic of the IWK Children's Hospital. It is possible that these children may have a higher than average incidence of developmental disorders than the population at large, resulting also in an increased level of fluctuating asymmetry. The use of this group as controls may therefore give a conservative estimate of the true odds ratios for developmentally delayed versus non-developmentally delayed children.

We have presented a preliminary study showing modest but suggestive odds ratios. It is our hope that these results will encourage other researchers to investigate the usefulness of fluctuating asymmetry as a risk marker for developmental disorders.

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